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10/589,557	01/23/2007	Takki Koide	3691-0135PUS1	8209

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EXAMINER	
NOAKES, SUZANNE MARIE	
ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
06/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/589,557	KOIDE, TAKKI	
	Examiner	Art Unit	
	SUZANNE M. NOAKES	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) *5 and 7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/23/07; 11/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply - Sequence*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-4 and 6 in the reply filed on 23 February 2009 is acknowledged. The traversal is on the ground(s) that it would not be burdensome to search both inventions and furthermore, Raines et al. does not destroy unity of invention because Raines et al. does not teach a peptide trimer of claim which is tethered to one another in the backbone direction. This is not found persuasive because it is asserted that Raines et al., however, do teach this element as "tethered" is interpreted broadly but reasonably as being even joined by the simplest of hydrogen bonds. However, even assuming *arguendo* that Raines et al. do not teach this element of claim 1, Ottl et al. as noted below do. Thus, unity of invention is lacking. Applicants should note, however, that rejoinder of the withdrawn method claims remains a possibility should the elected products be found allowable.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

2. Claims 1-7 are pending. Claims 5 and 7 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Thus, claims 1-4 and 6 are subject to examination on the merits.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 15 November 2006 and 23 January 2007 have been considered by the examiner. See initialed and signed PTO-1449's.

Specification/Drawings

Compliance with Sequence Rules

This application contains no sequence listing filed concurrently with said application. However, this application contains sequence disclosures that are encompassed by the definitions for amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Thus, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

The following Figures contain sequences that contain four or more consecutive amino acids without any corresponding SEQ ID NO: and/or no reference to any SEQ ID NO: in the Brief Description of the Drawings.

a) Figure 3, show an example of amino acid sequences of a peptide trimer and molecular aggregate comprised of said trimer which details four or more amino acid sequences in a defined sequence.

b) In Figure 6, a linear amino acid sequence which details a three amino acid sequences comprised of peptide trimers.

** In addition, pp. 13-14, 19-20 disclosed various sequences, however, said sequences have never been filed in electronic or paper copy format.

* Since the noted sequences are not found in any sequence listing, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO: by providing the followings: (1) a copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO:.

Claim Objections

4. Claims 1-4 and 6 are objected to because of the following informalities: Claim 1 can be improved with respect to form and clarity, for example by modifying the claim: "A peptide trimer comprising three peptides of the same chain length, wherein said peptides have the repeating unit of –(Gly-X-Y-)- as the fundamental structure and X- and -Y represent any amino acid residue and wherein said peptides are each tethered to one another such that they are shifted relative to one another in the backbone direction".

Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 and 6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn to peptide trimers of the same length made-up of tripeptides having the same fundamental repeating unit of Gly-X-Y and wherein the peptides are tethered to one another such that they are shifted relative to One another in the backbone direction. This, however, reads on naturally occurring collagen such as type I or type III collagen. For instance, the following is taught and known:

Boudko et al. (2008, JBC, 283(47):32580-89) teach the following what is well known regarding the structure of type III collagen (see p. 2, 2nd column, , :

> "All collagen molecules consist of three polypeptide chains, called α chains, which contain at least one region of repeating Gly-Xaa-Yaa sequences (1–2). In the collagen molecule, the three _ chains each fold into a polyproline II-like left-handed structure, and the three polyproline II-like chains twist around each other to form a right-handed superhelix, called the collagen triple helix (4–7). Critical to the formation of the triple helix is the presence of a glycine residue at each third position in the chain because this residue is the only one that can exist in the small space at the center of the triple helix (8). Each of the three chains therefore has the repeating structure Gly-Xaa-Yaa, in which Xaa and Yaa can be any amino acid but are frequently the imino acids proline in the Xaa position and hydroxyproline (Hyp) in the Yaa position. Because both proline and Hyp are rigid, cyclic imino acids, they limit rotation of the polypeptide backbone and thus contribute to the stability of the triple helix. Collagen polypeptides that lack Hyp can fold into a triple helical conformation at low temperatures, but the triple helix formed is not stable at mammalian body temperature (8). (See o, 32580, 2nd column, middle paragraph)."

> "Structurally, type III collagen is a homotrimer composed of three α1(III) chains and resembles other fibrillar collagens. A key feature in the formation of type III collagen is a so-called disulfide or cystine knot, which is located between the triple helical region and the C-terminal telopeptide (22-23). The knot is formed by three interchain disulfide bonds and it significantly stabilizes the triple helical structure. The stability imparted by the disulfide knot has been successfully used to produce collagenous peptides that otherwise would be too unstable to study (24-25). Production of these peptides involves the Cterminal extension by the *bis*-cysteinyl-sequence GPCCG, followed by air or glutathione oxidation at lower temperature under slightly basic conditions." (see p. 32581, 1st column, 3rd paragraph).

Ottl et al. (J. Pep. Sci., 1999, 5:103-110) further teach the following regarding collagen structures and what is already well known in the art (and that which has been established in the in the 1960's).

> The most abundant structural macromolecules present in the extracellular matrix are the collagens, a class of molecules derived from several multigene families. The collagen molecules are composed of three identical or of two or three different a-chains of primarily repeating Gly-Xaa-Yaa triplets that induce each single α-chain to adopt a lefthanded poly-Pro-II helix and the three chains to intertwine with a one-residue shift into a righthanded triple-helical coiled coil [1–3].

Further, it is noted that Koide et al. (2007) teach that about 1/3 (e.g. greater than 30%) of collagen sequences, Xaa is occupied by Pro and Yaa by Hyp (see Koide et al., Phil. Trans. R. Soc. B, 2007, 362: 1281-91 – see at p. 1281, 2nd column)

Since the type III collagen are made of "identical" peptides to form homotrimers wherein each α-peptide chain is made up of the repeats of Gly-Xaa-Yaa, said peptide chains will also be identical in length. Also, since type I collagen, for example, form heterotrimers with two cysteines in their cystine knots (e.g. in the α2 chain, whereas the α1 chain possesses one cysteine), and further, since said peptides for type I and type III collagen naturally form a triple helical structure which are facilitated and stabilized by interchain disulfide bonds, the instant claims read upon a product of nature and do not show the hand of man.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Barth et al. (Chem. Eur. J., 2003, 9: 3703-14).

The claims are drawn to a collagen-like peptide trimer, wherein each peptide is essentially comprised of the basic repeating unit of Gly-X-Y (wherein X and Y are any amino acid), and wherein said peptides are tethered to one another in the backbone direction (claim 1); via disulfide bonds (claim 2); wherein two of the peptides have one cysteine and the remaining peptide has two cysteines (claim 3); wherein the trimer as a whole has +30% of X being Pro and +30% of Y being Pro or Hyp (claim 4) and wherein said peptide trimer forms a molecular aggregate (claim 6).

Barth et al. teach synthetic homotrimeric collagen-like peptides comprised of the collagen tripeptide repeat (Xaa-Yaa-Gly), which is the same as Gly-Xaa-Yaa, which form peptides of the same length, possess two cysteine resides per peptide and which form disulfide bonds to tether the peptides to one another to form a stable triple helical structure via synthetic cystine knots (see Figures 1 and 2), and wherein the peptides are shifted relative to one another in the backbone direction (see Figure 2) and wherein Xaa is Pro and Yaa is Hyp and at least 30% of the amino acids of the tripeptide is Pro and Hyp, respectively (see Figures 1 and 2).

References of Interest - Not Relied Upon

8. Ottl et al. (JACS, 1999, 121:653-661) - teach collagen-like peptides (trimers) formed by the tripeptide repeat of $(Gly\text{-}Pro\text{-}Hyp)_n$, wherein n = 3 or 5, as the basic fundamental structure and where they have introduced an artificial cystine knot at the C-terminus. The three peptides align and are shifted relative to one another in the backbone direction (see Figure 1) according to the *α1α2α1'* formula, wherein the α2 peptide has two cysteine residues and the α1 and α1' peptide each comprise 1 cysteine residue. Two of the peptides are of the same length, the other peptide has one amino acid less.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656
27 May 2009